

## REMARKS

In response to the Office Action mailed June 1, 2006, Applicant has amended claims 12-14, 16, 19-23, 26-27 and 30-31. Claims 1-7, 15, 17-18, 24-25 and 28-29 have been canceled herein. It is urged that support for all the above amendments may be found throughout the specification as originally filed, including, *e.g.*, at page 4, line 7; page 34, lines 5-9; at page 37, line 29 through page 38, line 6; page 99, lines 13-15; page 54, lines 28-29; page 55, lines 5-6; page 81, lines 23-28; page 82, line 19; and elsewhere. No new matter has been added. The specification has been amended according to 37 C.F.R. § 1.57 to insert material that was previously incorporated by reference pertaining to the abbreviations objected to by the PTO. Support for “(formerly BST1; dihydrosphingosine-1-phosphate lyase 1)” can be found in the Lanterman and Saba reference, referred to in the specification as filed at page 85, line 6 and incorporated by reference in its entirety at page 18, lines 18-12. Support for “yeast sphingosine resistance 2” can be found in Mao *et al.*, referred to in the specification as filed at page 123, lines 12-14 and incorporated by reference in its entirety at page 18, lines 18-12. The present amendments are not to be construed as acquiescence with regard to the Examiner’s rejections and are made without prejudice to prosecution of any subject matter removed or modified by this amendment in a related divisional, continuation or continuation-in-part application. Following the amendments, claims 12-14, 16, 19-23, 26-27 and 30-31 are pending in the application. Favorable reconsideration of the subject application is respectfully requested in view of the above amendments and the following remarks.

### ***Claim Objections***

Claims 2-7, 13, 15, 17-19, 21, 23-26 and 28-31 stand objected to as allegedly containing abbreviations that were not fully set forth at least once prior to their use. The Action asserts that the meanings of the abbreviations DPL1, LCB4, SPHK1, LCBP, S-1-P and YSR2 should be set forth fully prior to use.

Without acquiescing to the objection, Applicant has amended the claims to recite in full the meanings of these abbreviations prior to their use. Applicant submits that the skilled artisan would readily recognize that these abbreviations refer to the genetic loci as recited in the

claims in view of the teachings of the specification as filed, for example at page 4, line 7; page 34, lines 5-7; page 82, line 19; page 85, line 6 (Lantermann and Saba reference, incorporated by reference at page 18, lines 18-12); page 123, lines 12-14 (Mao *et al.* reference, incorporated by reference at page 18, lines 18-22). Additionally, these abbreviations are well known in view of the teachings available in the art, such as the publicly available yeast genome database at [www.yeastgenome.org](http://www.yeastgenome.org). For the purposes of clarity, Applicant has amended the specification to expressly recite in full the terms for which the abbreviations DPL1 and YSR2 stand. As noted above, support for this amendment can be found in the Lantermann and Saba, and the Mao *et al.* references, both previously incorporated by reference in their entirety at page 18, lines 18-22 of the specification as filed. No new matter has been added. Applicant submits that the objection has been obviated in view of the amendments.

***Claim Rejections – 35 U.S.C. § 112, first paragraph (written description)***

Claims 1-7 and 12-31 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking written description. In particular, the PTO asserts that the specification lacks description of representative species encompassed by the genus of DNAs used in the methods of the claims. As such, the PTO asserts that the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that Applicant was in possession of the claimed invention at the time of filing.

Without acquiescing to the rejection and solely to advance prosecution, Applicant has canceled claims 1-7, 15, 17-18, 24-25, 28-29 and amended the remaining claims to specifically recite "...the mutant yeast strain comprises a null allele of at least one gene encoding a component of a sphingolipid pathway that results in an altered activity level of at least one sphingolipid pathway component, wherein said at least one gene comprises a DPL1 gene and a LCB4 gene and wherein said mutant strain of yeast has been genetically altered to express at least one nonendogenous SK, and wherein the mutant yeast strain exhibits growth inhibition in the presence of sphingosine...". These amendments are made without prejudice to prosecution of any subject matter removed or modified by this amendment in a related divisional, continuation or continuation-in-part application. Reconsideration of the amended claims and withdrawal of the rejection are respectfully requested.

***Claim Rejections – 35 U.S.C. § 112, first paragraph (enablement)***

Claims 1-7 and 12-31 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement. In particular, in the Action the PTO asserts that the specification, while being enabling for a method of identifying an agent that modulates sphingolipid metabolism using a mutant *Saccharomyces cerevisiae* strain comprising a null allele of the endogenous DPL1 gene and/or LCB4 gene and/or YSR2 gene and transforming said mutant strain with the human SPHK1 gene, does not reasonably provide enablement for such a method using any mutant yeast strain comprising null alleles of any gene encoding any component of a sphingolipid pathway and expressing any non-endogenous gene of the sphingolipid pathway.

Without acquiescing to the rejection and solely to advance prosecution, Applicant has canceled claims 1-7, 15, 17-18, 24-25, 28-29 and amended the remaining claims to specifically recite "...the mutant yeast strain comprises a null allele of at least one gene encoding a component of a sphingolipid pathway that results in an altered activity level of at least one sphingolipid pathway component, wherein said at least one gene comprises a DPL1 gene and a LCB4 gene and wherein said mutant strain of yeast has been genetically altered to express at least one nonendogenous SK, and wherein the mutant yeast strain exhibits growth inhibition in the presence of sphingosine...". These amendments are made without prejudice to prosecution of any subject matter removed or modified by this amendment in a related divisional, continuation or continuation-in-part application. Reconsideration of the amended claims and withdrawal of the rejection are respectfully requested.

***Claim Rejections – 35 U.S.C. § 103***

Claims 1-7 and 12-31 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Lanterman *et al.* (Biochem J. 1998 Jun 1; 332 (Pt 2):525-31), Kim *et al.* (Genetics 2000 Dec; 156(4):1519-29) and in view of Melendez *et al.* (Gene. 2000 Jun 13; 251(1):19-26 and GenBank Accession No. AF266756, created 6/1/2000). In particular, the PTO asserts in the Action that Lanterman *et al.* teach the creation of a yeast mutant strain comprising a null allele of the DPL1 gene, which strain is sensitive to sphingosine owing to its inability to degrade S-1-P. Lanterman *et al.* allegedly further teach that in double mutants where the LCB4 gene has also

been knocked out, the mutant strain is no longer sensitive to sphingosine since the LCB4 kinase is no longer producing the S-1-P. The PTO concedes that Lanterman *et al.* do not teach a mutant yeast strain comprising a null allele of endogenous YSR2 and transforming said mutant strain with non-endogenous SK. The PTO asserts that Kim *et al.* and Melendez *et al.* overcome this deficiency while further conceding that neither Lanterman *et al.* nor Kim *et al.* teach methods of screening agents using a yeast system as presently claimed. The PTO relies on Melendez *et al.* as allegedly remedying this deficiency. As such, the PTO alleges that it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Lanterman *et al.*, Kim *et al.*, and Menendez *et al.* to arrive at Applicant's invention.

Applicant respectfully traverses the rejection on the following grounds.

In the Action the PTO fails to establish a *prima facie* case of obviousness. (*See In re Mayne*, 104 F.3d 133, 1341-43, 41 U.S.P.Q.2d 1451 (Fed. Cir. 1997) (PTO has the burden of showing a *prima facie* case of obviousness.)). The Examiner must show (1) that the combined references teach or suggest all claim limitations; (2) that the references provide some teaching, suggestion, or motivation to combine or modify the teachings of the prior art to produce the claimed invention; and (3) that the combined teachings of the references indicate that by combining the references, a person having ordinary skill in the art will achieve the claimed invention with a reasonable expectation of success. When rejection of claims depends upon a combination of prior art references, a teaching, motivation, or suggestion to combine the references must exist. (*See In re Rouffet*, 149 F.3d 1350, 1355, 47 U.S.P.Q.2d 1453 (Fed. Cir. 1998)).

At the time of filing the present application, the cited combination of references would not have motivated a person having ordinary skill in the art to arrive at the claimed invention with the requisite reasonable expectation of success. In particular, Applicant submits that Lanterman *et al.* merely describe the characterization of sphingosine kinase activity in *Saccharomyces cerevisiae*. As admitted by the PTO in the Action, nowhere does this reference teach the presently disclosed mutant yeast strains expressing a non-endogenous SK protein as recited in the instant claims. For reasons given below, the Action relies improperly on Kim *et al.* and Melendez *et al.* to overcome this deficiency.

Kim *et al.* merely describe the further characterization of the biological role of phosphorylated long chain bases in yeast. Kim *et al.* fail to cure the deficiencies of Lanterman *et al.*, in particular by providing no actual teaching with regard to the use of nonendogenous SK in a screening assay. Melendez *et al.* merely teach the molecular cloning and characterization of the human SK cDNA with no teaching of the use of such a cDNA as a nonendogenous gene in a yeast screen and, in fact, no teaching whatsoever of any screening methods. Applicant submits that the Action employs inappropriate and selective hindsight where the allegation of obviousness is asserted to derive from a reason in the art other than knowledge provided by Applicant's disclosure. *In re Dow Chemical Co.*, 837 F.2d 469; 5 USPQ2d 1529 (Fed. Cir. 1988). Absent the teachings of the present application, the documents cited in the Action simply fail to render the claimed invention obvious to the person having ordinary skill in the art, who would have no basis for reasonably believing that the instant methods could be successfully practiced.

In alleging that there would have been motivation to combine the references to arrive at a method to screen modulators of sphingolipid metabolism, at best, the Action asserts nothing more than that it would have been "obvious to try." Such an assertion cannot be regarded as a conclusory finding that the claimed invention is obvious, and in fact fails to support a *prima facie* case of obviousness. *In re Eli Lilly & Co.*, 902 F.2d 943; 14 USPQ2d 1741 (Fed. Cir. 1990).

Accordingly, Applicant submits that the primary and secondary references, taken individually or for what they teach as a whole, do not teach or suggest the claimed invention. Therefore, Applicant submits that the claimed invention would not have been obvious to the ordinarily skilled artisan at the time of filing. Reconsideration and withdrawal of the rejection are respectfully requested.

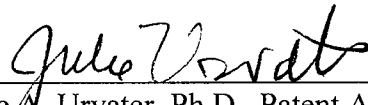
Application No. 10/622,011  
Reply to Office Action dated on June 1, 2006

In view of the above amendments and remarks, the claims are now believed to be in condition for allowance. However, should any further issue require attention prior to allowance, the Examiner is requested to contact the undersigned at 206-622-4900 to resolve same.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,

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